chloric acid. The mixture was boiled for five hours; a small amount of an oily phase was observed at the end of the period. Dilution with water, extraction of the precipitated partly crystalline material with ether, treatment with diazomethane, and evaporation gave 465 mg. (95%) of crude methyl 11-ketocholanate, m.p. about 75–84°. Chromatography on alumina gave 325 mg. (67%) in 10 fractions, which were further purified by recrystallization from dilute methanol. The keto ester forms square prismatic needles, m.p. 89.4–90.5°; $[\alpha]^{20}_{D}$ +48.1 ± 2° (2.10% an).[5]

Anal. Calcd. for $C_{25}H_{40}O_3$ (388.57): C, 77.27; H, 10.38. Found: C, 76.94; H, 10.41.

Other reducing agents such as zinc and ammonia, hydrogen iodide and phosphorus, zinc amalgam or magnesium amalgam in toluene, sodium amalgam in aqueous medium, either led to intractable products or recovery of starting material when applied to attempted reduction of Va, Vb or Vd.

Dehydration of Methyl 3α-Acetoxy-9α,11β-dihydroxycholanate (XI) to Methyl 3α-Acetoxy-11-ketocholanate (XXII).—Dry hydrogen bromide was passed into a solution of 297 mg. of XI in 5 cc. of alcohol-free chloroform for 20 minutes at room temperature. The solution became slightly cloudy owing to the water liberated. The solvent was removed in vacuum and the residue dissolved in benzene, which was distilled in like manner. The solid residue (m.p. 120–125°) was recrystallized from aqueous acetone, which deposited 183 mg. (64%) of XXII, m.p. 124–129°. Further purification raised the melting point to 131.2–132.6°, not depressed by an authentic sample of XXII[32]; $[\alpha]^{23}_{D}$ +67.9 ± 2° (2.21% an).

In a similar experiment the yield of XXII melting at 129.6–131.4° was 55%. Other reagents that also accomplish the dehydration are boron fluoride etherate, hydrogen bromide (32%) in acetic acid, or sulfuric acid in warm acetic acid, but the yields are poor. Hydrogen chloride in chloroform does not bring about the reaction.

The mother liquor from the dehydration described in detail contained halogenated material (Beilstein test) that proved to be intractable. In one boron fluoride catalyzed dehydration the total crude product was chromatographed; the most easily eluted fractions gave, after recrystallization, 36% of pure XXII, m.p. 131.5–134.0°; the more strongly adsorbed material did not crystallize, and no conclusions as to its nature could be drawn from an infrared spectrum.

CAMBRIDGE, MASSACHUSETTS RECEIVED APRIL 20, 1951

[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1a]]

Preparation of Esters by Reaction of Ammonium Salts with Alcohols[1b]

BY E. M. FILACHIONE, E. J. COSTELLO AND C. H. FISHER[2]

A modified esterification procedure by which ammonium salts of organic acids react with alcohols to produce esters and ammonia was investigated. This reaction seems to be generally suitable for the preparation of esters of organic acids. Similarly, reaction of amine salts with alcohols gives ester and amine. This method of esterification may be useful for preparing esters from acid-sensitive alcohols and organic acids as well as for preparing esters of certain fermentation acids.

Ammonium salts of organic acids differ markedly from metallic salts in chemical properties. When heated, ammonium salts are converted into amides, accompanied by dissociation into ammonia and the acid.[3] Ammonium salts have been distilled under vacuum, partial dissociation into an acid salt ($RCOONH_4 \cdot RCOOH$) taking place; the acid salt distilled as a pure compound.[4,5]

Other investigators have reported the reaction of ammonium salts with an excess of formaldehyde to liberate the free acid in quantitative yield,[6] and more recently the reaction of ammonium and substituted ammonium salts with diazomethane to produce the methyl ester and ammonia or amine, respectively,[7] has been reported.

In this paper, we describe another novel reaction of ammonium and amine salts of organic acids, namely, the interaction between these salts and alcohols to produce an ester and ammonia or an amine.

$$RCOONH_4 + R'OH \rightleftarrows RCOOR' + NH_3 + H_2O$$

The reaction bears some resemblance to direct esterification, and from an over-all viewpoint may be considered a direct esterification of ammonium salts with alcohols. This method of producing esters, therefore, may be of interest, particularly where the acidic conditions of conventional esterification are deleterious to the reactants as well as in preparing esters of certain fermentation acids.

As far as we can ascertain, there is no mention in the literature that ammonium salts as such are capable of undergoing an esterification type of reaction. There are many instances in which ammonium salts of organic acids have served as starting material for the preparation of esters, but in each case the organic acid was first liberated by addition of equivalent amounts of a strong mineral acid.

These reactions of ammonium salts are typical reactions of either carboxylic acid (the reactions with diazomethane or alcohols), or of ammonia (the reaction with formaldehyde). Perhaps they may be best explained on the basis of dissociation of the salt into acid and ammonia or amine.

The ammonium salts were esterified by refluxing the mixture of ammonium salt and alcohol under conditions permitting continuous removal of both ammonia and water from the reaction mixture. This was conveniently accomplished by using an entraining agent, which in most cases was the alcohol used in the reaction. When water-soluble alcohols were used toluene or some other suitable solvent was added to serve as an entraining agent. Esterification of amine salts was carried out in the

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[1] (a) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted. (b) Presented in part at the 116th A. C. S. Meeting held in Atlantic City, N. J., Sept. 1949, and also at the Miniature meeting of the Philadelphia Section of the American Chemical Society held in Philadelphia, Pa., in January, 1949.

[2] Southern Regional Research Laboratory, New Orleans, La.

[3] C. D. Hurd, "Pyrolysis of Carbon Compounds," A. C. S. Monograph 50, Reinhold Publishing Corp., New York, N. Y., 1929, page 507.

[4] R. Reik, *Monatsh.*, **23**, 1033 (1902).

[5] R. Escales and H. Koepke, *J. prakt. Chem.*, **87**, 258 (1913).

[6] A. Ronchèse, *J. pharm. chim.*, **25**, 611 (1907); *Analyst*, **32**, 303 (1907).

[7] M. Frankel and E. Katchalski, THIS JOURNAL, **65**, 1670 (1943); *ibid.*, **66**, 763 (1944).

TABLE I

ESTERIFICATION OF AMMONIUM SALTS

Expt. no.	Reactants NH_4 salt	Mole	Alcohol	Moles	Temp.,[a] °C.	Time, hr.	Conversion, % Ester	NH_3	Free acid
1	Acetate	1.0	*n*-Butyl	2.5	118–122	7.5	64	88	23
2	Acetate	1.0	*n*-Hexyl	2.5	142–158	2.5	70	86	18
3	Acetate	0.5	Furfuryl[b]	0.55	103–121	3.0	<20	56	
4	Propionate	1.0	*n*-Butyl	2.5	99–126	2.5	23	92	64
5	2-Ethylhexanoate	1.0	*n*-Butyl	2.5	98–131	3.5	0	94	95
6	Crotonate	1.0	Crotyl[b]	1.0	90–118	8.5	12	80	16
7	Benzoate	1.0	*n*-Amyl	2.0	97–159	14.2	42	80	52
8	Adipate	1.0	*n*-Butyl	4.0	97–139	14.3	50	87	
9	Phthalate	0.5	*n*-Butyl	4.0	95–121	9.5	0[c]	51	
10	Glycolate	1.0	*n*-Butyl	2.5	102–130	6.0	27[d]	45	
11	Glycolate	1.0	2-Methylpentyl	2.5	108–160	4.0	22[d]	52	
12	Glycolate	1.0	3-Heptyl	2.5	111–180	5.8	0	38	
13	Glycolate	1.0	2-Ethylhexyl	2.5	111–182	6.0	68	87	
14	Lactate	1.0	*n*-Butyl	2.5	106–134	7.0	49	87	
15	α-Acetoxypropionate	1.0	*n*-Butyl	2.5	98–146	5.0	19[e]	82	11
16	α-Hydroxyisobutyrate	1.0	*n*-Butyl	2.5	95–133	5.0	14	73	
17	Citrate	0.5[f]	*n*-Butyl	2.5	108–128	6.5	0[f]	12	
18	Salicylate	0.5	Isoamyl	2.2	138–143	5.0	0	80	70–95
19	Control:acetic acid	1.0	*n*-Butyl	1.4	111–121	6.5	67	..	
20	Control:lactamide	1.0	*n*-Butyl	2.5	123–137	8.5	0	3	

[a] Initial and final temperatures of the reaction mixture. [b] Toluene (100–200 ml.) was used as an entraining agent. [c] Phthalimide (100% yield) was obtained. [d] Glycolamide (35% yield) was also formed. [e] 30% conversion to butyl lactate. [f] T. H. Easterfield and W. J. Sell, obtained citrazinic acid upon heating diammonium citrate, *J. Chem. Soc.*, **65**, 29 (1894).

same manner. However, the amine produced, being non-volatile, remained in the reaction mixture; water was the only component removed by the entraining agent.

In several instances, conversion to ester was reasonably satisfactory—40 to 70% (Table I) in the case of ammonium acetate, benzoate, adipate, lactate and glycolate. No ester was obtained from ammonium salicylate, citrate, phthalate and 2-ethylhexanoate. In general more than 80% was converted to ammonia, indicating that formation of amide was not an important side reaction. Free acid as well as ester was produced, and in some cases the free acid was the predominating reaction product. Amine salts, particularly those of tertiary amines, appeared equally suitable for the preparation of esters.

The fact that the esterification does not occur through the amide as an intermediate seems to be clearly indicated by the absence of ester and ammonia formation when lactamide was refluxed with butanol under the same conditions which produced butyl lactate from ammonium lactate.

Reaction of ammonium acetate with butyl alcohol seemed to be comparable to the non-catalyzed esterification of acetic acid with butyl alcohol, as shown by comparing Experiments 1 and 19 of Table I. Under approximately the same experimental conditions, substantially identical conversion into ester was obtained.

In general the primary alcohols were better suited for this reaction than the secondary alcohols. The amine salts, except primary aliphatic amine salts, behaved in the same manner as the ammonium salts.

Experimental

Salts.—Ammonium acetate and salicylate and diammonium citrate were commercially available salts. The other salts were prepared by neutralizing the appropriate acid with an equivalent amount of ammonia or an amine.

Esterification of Ammonium Salts.—The esterification procedure was essentially that described for esterification of ammonium acetate with *n*-butyl alcohol. A mixture of 1.0 mole of ammonium acetate, either solid or in a concentrated aqueous solution and 2.5 moles of *n*-butyl alcohol was refluxed in an apparatus conventionally used in esterification reactions to displace the equilibrium by removal of water. The vapors from the refluxing reaction mixture were led through a 2-foot column (1-inch diameter) packed with short lengths of glass tubing and condensed over a modified Dean and Stark water-separating trap. The two-phase condensate collected in the trap, and the upper layer was automatically returned to the reaction flask, and the lower water layer, containing some ammonia, was periodically withdrawn. The non-condensable vapor, mainly ammonia, was led into boric acid solution to absorb the remaining ammonia. A safety trap containing a small amount of water was necessary to prevent the boric acid solution from being drawn back into the reaction flask. Total ammonia was determined by titration of the combined aqueous solutions containing ammonia.[8]

During the reaction, the temperature of the refluxing vapor rose from approximately the boiling point of the alcohol–water azeotrope to the boiling point of the alcohol. Refluxing was continued until the removal of water virtually ceased, which in general required 5 to 10 hours in the esterification reactions employing the lower boiling alcohols.

The temperature of the reaction mixture, when an aqueous solution of the ammonium salt was esterified with butyl alcohol, was approximately 100° initially and rose to a final value in the range 120–150°. Higher temperatures of the reaction mixture resulted when higher boiling alcohols were employed.

When reaction was considered terminated, the ester was isolated from the mixture by distillation in vacuum (Table I, Experiments 1, 2, 4, 5, 6 and 13). In other cases, the reaction mixture was first washed with water or cold dilute alkali prior to distillation.

The esters of acetic and propionic acid distilled azeotropically with the alcohol, and the distillate also contained free acid. In these experiments, the conversion into free acid was determined by titration and conversion into ester by saponification.

The results obtained in the esterification of ammonium

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[8] E. C. Wagner, *Ind. Eng. Chem., Anal. Ed.*, **12**, 771 (1940).

TABLE II

ESTERIFICATION OF SUBSTITUTED AMMONIUM SALTS

Expt. no.	Reactants Salt	Mole	Alcohol	Mole	Temp.,[a] °C.	Time, hr.	Conversion, % Ester	Amine
1	Quinoline acetate	1.0	*n*-Butyl	1.0	133–149	3.6	46[b]	...
2	Diamylamine acetate	0.5	*n*-Butyl	0.55	143–168	9.5	32	44
3	Dihexylamine acetate	0.5	Furfuryl[c]	0.55	139–166	17.5	10	58
4	Triamylamine acetate	0.5	*n*-Butyl	0.55	142–165	10.0	62[d]	94
5	Trihexylamine acetate	0.5	Furfuryl[c]	0.55	140–158	24.5	30[e]	90
6	Aniline lactate	1.0	*n*-Hexyl	2.5	119–174	2.0	33	48
7	Decylamine lactate	0.34	*n*-Butyl	0.85	115–158	7.0	0[f]	0[f]
8	Dihexylamine lactate	0.5	*n*-Butyl	1.25	119–155	11.5	40	72
9	Tributylamine lactate	0.5	*n*-Butyl	1.25	110–163	5.5	68	...
10	Triamylamine lactate	0.5	*n*-Butyl	1.25	109–152	5.5	42	...
11	Trihexylamine lactate	0.5	*n*-Butyl	1.25	116–157	11.5	78	72[g]

[a] Initial and final temperatures of the reaction mixture. [b] 39% conversion to acid. [c] Toluene, 75–100 ml., was used as an entraining agent. [d] 22% conversion to free acid. [e] 50% conversion to free acid. [f] 68% conversion to *n*-decyllactamide. [g] Isolated by distillation in nitrogen.

salts of various types of organic acids are summarized in Table I.

Esterification of Amine Salts.—The procedure for esterification of amine salts with alcohols was similar to that described for esterification of ammonium salts. The temperature of the refluxing reaction mixture was generally higher than that for the ammonium salt esterifications. Water was the only component removed from the reaction mixture during esterification; the amines formed during the reaction, being high boiling, remained in the reaction mixture. The ester was isolated by distillation of the reaction mixture in vacuum.

Table II summarizes the esterification of various amine acetates and lactates with butyl and furfuryl alcohols. Excepting Experiments 3 and 7, conversion of amine salt to ester and to amine ranged from 30 to 78 and 44 to 94%, respectively.

2-Methylpentyl glycolate, a new compound, had the following properties: b.p. 66° at 1.2 mm.; n^{20}_D 1.4340; d^{20}_4 0.9864.

Anal. Calcd. for $C_8H_{16}O_3$: C, 59.97; H, 10.07; sapn. equiv., 160.2. Found: C, 60.13; H, 10.12; sapn. equiv., 160.7.

2-Ethylhexyl glycolate: The properties of this previously undescribed ester were: b.p. 94° at 2.2 mm.; n^{20}_D 1.4400.

Anal. Calcd. for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71; sapn. equiv., 188.3. Found: C, 63.92; H, 10.72; sapn. equiv., 188.7.

The authors are indebted to C. O. Willits and co-workers for the analytical data.

PHILADELPHIA 18, PENNA. RECEIVED MAY 19, 1951

[CONTRIBUTION FROM THE SHELL DEVELOPMENT COMPANY]

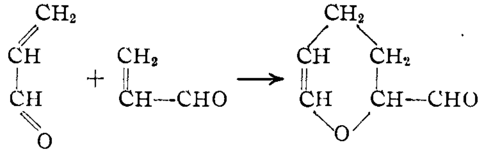
Reactions of Acrolein and Related Compounds. I. Addition of Vinyl Ethers

BY CURTIS W. SMITH, DOUGLAS G. NORTON AND SEAVER A. BALLARD

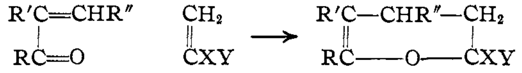
Simple thermal addition of acrolein and vinyl ethers has given the versatile 2-alkoxy-dihydropyrans in high yield. Divinyl ether, phenyl vinyl sulfide, methacrolein and crotonaldehyde also add to give 3,4-dihydro-2H-pyrans substituted in the 2- rather than the 3-position. The reaction is not reversible at 180° in the liquid phase; however, at 400° in the vapor phase 2-isobutoxy-3,4-dihydro-2H-pyran did revert in high yield to its antecedents, isobutyl vinyl ether and acrolein.

Introduction

The thermal dimerization of acrolein[1] and other conjugated carbonylic compounds involves the addition of one molecule activated at the carbon–carbon double bond to another molecule activated at the 1,4-positions of the conjugated system.



The addition has a formal similarity to the Diels–Alder reaction in that the conjugated carbonylic compound functions both as a diene (1,4-addition) and as a dienophile (1,2-addition). It was of interest to determine whether this reaction could be generalized to the extent that other 1,2-addenda could be found which would add to acrolein in the 1,4-positions. This objective has been achieved in the sense that quite a wide variety of ethylenic compounds have been added to acrolein and other conjugated carbonylic compounds in the desired manner to give a series of dihydropyrans.[2]



$$\begin{matrix} R'C{=}CHR'' & CH_2 & & R'C{-}CHR''{-}CH_2 \\ | & \| & \longrightarrow & | \qquad\qquad\qquad | \\ RC{=}O & CXY & & RC{-}O{-}CXY \end{matrix}$$

The presentation of these addition reactions has been divided into three parts: I, addition of vinyl ethers; II, addition of unsaturated esters, and methacrylonitrile; III, addition of olefins. A discussion of the reaction mechanism is presented in the third paper. As shown in the above equation, orientation during reaction is such that 2- rather than 3-substituted dihydropyrans are formed.

Vinyl alkyl ethers[3] react rapidly and in high

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(1) K. Alder and E. Ruden, *Ber.*, **74**, ,920 (1941); K. Alder, H. Offermans and E. Ruden, *ibid.*, **74**, 905 (1941).

(2) C. W. Smith, D. G. Norton and S. A. Ballard, U. S. Patent 2,514,168 (1950).

(3) Since this paper was presented at the Philadelphia Meeting of the American Chemical Society, Division of Organic Chemistry, April 9, 1950, a paper on the addition of vinyl ethers to conjugated carbonylic compounds has been published by R. I. Longley and W. S. Emerson, THIS JOURNAL **72**, 3079 (1950). More recently Parham and Holmquist (*ibid.*, **73**, 913 (1951)) have presented the addition of vinyl *n*-butyl ether to crotonaldehyde.